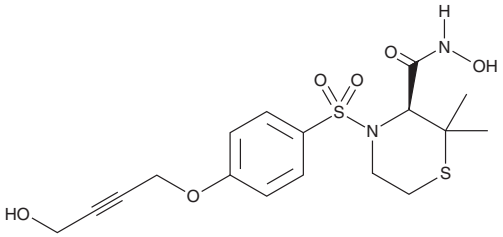
PRODUCT INFORMATION

TMI-005

Item No. 29016

CAS Registry No.:	287405-51-0
Formal Name:	(3S)-N-hydroxy-4-[[4-[(4-hydroxy-2-butyn-1-yl)oxy]phenyl]sulfonyl]-2,2-dimethyl-3-thiomorpholinecarboxamide
Synonym:	Apratastat
MF:	$C_{17}H_{22}N_2O_6S_2$
FW:	414.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 242 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

TMI-005 is supplied as a crystalline solid. A stock solution may be made by dissolving the TMI-005 in the solvent of choice, which should be purged with an inert gas. TMI-005 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of TMI-005 in ethanol is approximately 10 mg/ml and approximately 25 mg/ml in DMSO and DMF.

TMI-005 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, TMI-005 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. TMI-005 has a solubility of approximately 0.02 mg/ml in a 1:40 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

TMI-005 is an inhibitor of disintegrin and metalloproteinase domain-containing protein 17/TNF-α converting enzyme (ADAM17/TACE), matrix metalloproteinase-1 (MMP-1), and MMP-13 (IC_{50}s = 20, 33, and 8.1 nM, respectively).[1] It inhibits LPS-induced TNF-α release in isolated human whole blood (IC_{50} = 144 ng/ml).[2] TMI-005 (25 µM) reduces basal and ionizing radiation-induced secretion of the ADAM17/TACE substrates ALCAM and amphiregulin from A549 and NCI H125 cells.[3] It inhibits proliferation of A549 cells when used at concentrations of 25 and 50 µM and sensitizes A549 and NCI H125 cells to ionizing radiation at 25 µM. TMI-005 (25 mg/kg twice per day) reduces tumor growth in an A549 mouse xenograft model when administered in combination with ionizing radiation.

References

1. Levin, J.I., Chen, J.M., and Cole, D.C. Acetylenic α-amino acid-based sulfonamide hydroxamic acid tace inhibitors. *American Cyanamid Company.* **WO 00/44709** (2000).
2. Shu, C., Zhou, H., Afsharvand, M., *et al.* Pharmacokinetic-pharmacodynamic modeling of apratastat: A population-based approach. *J. Clin. Pharmacol.* **51(4),** 472-481 (2011).
3. Sharma, A., Bender, S., Zimmerman, M., *et al.* Secretome signature identifies ADAM17 as novel target for radiosensitization of non-small cell lung cancer. *Clin. Cancer Res.* **22(17),** 4428-4439 (2016).

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